Membranous Nephropathy

Challenges in diagnostics and treatment

Akademisk avhandling
som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin vid Göteborgs universitet kommer att offentligen försvaras i Hjärtats aula, Vita stråket 12, Sahlgrenska Universitetssjukhuset/Sahlgrenska, Göteborg,
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av
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Fakultetsopponent:
Professor Stefan Jacobson, Karolinska Institutet, Stockholm

Avhandlingen baseras på följande delarbeten:

I. **Glomerular IgG subclasses in idiopathic and malignancy-associated membranous nephropathy**
Jennie Lönnbro Widgren, Kerstin Ebefors, Johan Mölne, Jenny Nyström and Börje Haraldsson.
Clinical Kidney Journal 2015 Aug;8(4):433-9; doi:10.1093/ckj/sfv049.

II. **Treatment pattern in patients with idiopathic membranous nephropathy - practices in Sweden at the start of the millennium**
Jennie Lönnbro Widgren, Johan Mölne, Börje Haraldsson and Jenny Nyström.
Clinical Kidney Journal 2016; doi: 10.1093/ckj/sfv152

III. **Initial anti-phospholipase A2 receptor antibody levels predict clinical outcome in patients with idiopathic membranous nephropathy**
Jennie Lönnbro Widgren, Kerstin Ebefors, Barbara Seitz-Polski, Christine Payré, Gérard Lambeau, Johan Mölne, Börje Haraldsson and Jenny Nyström.
Submitted

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Abstract

The variability in the pathogenesis, clinical presentation and outcome of membranous nephropathy (MN) poses major clinical challenges and raises different questions, both regarding diagnostics and treatment of patients with MN. The aims of this thesis were therefore to examine: 1) differences in the glomerular expression of different IgG subclasses and phospholipase A2 receptor (PLA_2R) between patients with idiopathic and malignancy-associated MN; 2) treatment pattern of patients with idiopathic MN; and 3) if the serum PLA_2R antibody level at diagnosis can be used as a prognostic marker.

We found that absence of glomerular IgG4 and PLA_2R indicates malignancy-associated MN. IgG2 was present in a large number of patients of both groups, and could not be used as an indicator of an underlying malignancy. Moreover, in our material we found no evidence for an IgG subclass switch during the disease process, as IgG1 and IgG3 were present in a low number of patients.

When investigating the treatment pattern of patients with idiopathic MN, we found that a majority of the patients (75%), had reached remission at the study end. 10% had developed end-stage renal disease, a fairly high number, given that 51% of the patients received immunosuppressive therapy at some point, and that 88% of the patients received supportive treatment with ACEIs and/or ARBs. The specific treatment varied, and there was a tendency to start treatment at an early point (21% of the patients) instead of awaiting a spontaneous remission. Not recommended therapy was used in a high proportion of these cases (47%).

In a retrospective cohort of patients with saved blood samples from the time of renal biopsy, we found a significant correlation between a high serum PLA_2R antibody level at presentation, and a less favorable clinical outcome. Patients with higher autoantibody levels were more exposed to immunosuppressive therapy, but still there were less cases of complete remission among these patients.

We conclude that absence of glomerular IgG4 and PLA_2R should raise the question of an underlying malignancy in a patient with MN. Moreover, the serum PLA_2R antibody level at presentation seems to be the prognostic marker urged for, in the decision of whom and when to treat with immunosuppressive therapy.

Keywords: Glomerulonephritis, membranous nephropathy, proteinuria, phospholipase A2 receptor, cancer, end-stage renal disease

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